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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,773	03/23/2005	Tadashi Yoneda	Q72135	6335
23373	7590	02/27/2009	EXAMINER	
SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			UNDERDAHL, THANE E	
			ART UNIT	PAPER NUMBER
			1651	
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			02/27/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/528,773

**Applicant(s)**

YONEDA ET AL.

**Examiner**

THANE UNDERDAHL

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 11-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CDC)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

Detailed Action

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/08/08 has been entered.

This Office Action is in response to the Applicant's request for continued examination received 12/08/08. Claims 1-20 are pending. Claims 11-20 are withdrawn. No claims are cancelled. No claims have been amended. No claims are new.

**Response to Applicant's Arguments**

In the response submitted by the Applicant the 35 U.S.C § 102 (b) rejection of claims 1-10 based on Ohno #1 as the primary reference is withdrawn in light of Applicant's argument.

**New Rejections**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, and 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ a specific strain of *Bacillus subtilis*. It is not clear if the written description is sufficiently repeatable to avoid the need for a deposit. Further it is unclear if the starting materials were readily available to the public at the time of invention.

It appears that a deposit was made in this application as filed as noted on page 8, lines 19-25 of the specification. However, it is not clear if the deposit meets all of the criteria set forth in 37 CFR 1.801-1.809. Applicant or applicant's representative may provide assurance of compliance with the requirements of 35 U.S.C § 112, first paragraph, in the following manner.

#### SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection and rejection based on a lack of availability of biological material.

1. Identifies declarant.
2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.
3. States that the deposited material has been accorded a specific (recited) accession number.
4. States that all restriction on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.
5. States that the material has been deposited under conditions that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 U.S.C § 122.

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit for the enforceable life of the patent, whichever period is longer.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure (e.g. see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository and the complete taxonomic description.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phae et al. (J. Fermentation And Bioengineering, 1991) in light of support of Tulin et al. (BIOTECHNOLOGY AND BIOENGINEERING, 1992), DeMain et al. (J Bacteriol. 1958) and Gary et al. (J. Bacteriol. 1952).

These claims are to a method of producing Iturin A comprising the following steps:

- o Cultivating a *Bacillus* microbe with the ability to produce **Iturin A (ItA)** or its homologues;
- o The medium contains 2% mass or more of soybean powder or its extract
- o The microbe produces ItA and its homologues in the medium to a concentration of 1.5 g/L or more.

The claims further limit that the *Bacillus* microbe continues to grow when iturin A and its homologs are produced to a concentration of at least 1.5 g/L that is accumulated in the medium. The *Bacillus* microbe produces 50 ppm or less of surfactin in the medium during cultivation. The medium contains 3% mass or less of  $K_2HPO_4$ . The *Bacillus* is further limited to *Bacillus subtilis* SD142 or a mutant thereof. The medium also contains supplements such as maltose, starch syrup, soluble starch, dextrin, glucose, sucrose, and fructose. The solid ItA or its homologues are obtained by drying the culture as claimed in claim 9.

Phae et al. teach that *B. subtilis* NB22 can be fermented in no. 3 medium which is a liquid medium that contains polypepton, glucose and  $KH_2PO_4$  (Phae, pg 118, Materials and Methods) to produce and accumulate ItA (See Abstract). The polypepton concentration can be as high as 50 g/L, which is about 5% (Phae, pg 121, col 1 line 8). One of ordinary skill in the art would realize that polypepton is an extract of soybeans as supported by Tulin et al. (pg 846, col 2, Different Polypepton Sources) The amount of  $KH_2PO_4$  added to the solution was 1g/L which calculates to a %mass of 0.1% (Phae, pg

118, col 1, Materials and Methods). It is well known in the art that both  $K_2HPO_4$  and  $KH_2PO_4$  are well known nutrients for *Bacillus subtilis*, as supported by Gary et al. (pg 501, Methods) and DeMain et al. (pg 517, col 2, Mineral Salt Mixture). Knowing this it would be obvious to one of ordinary skill in the art to substitute  $K_2HPO_4$  for  $KH_2PO_4$  or vice versa since both are known in the art for the same purpose (M.P.E.P. § 2144.06 II).

Phae et al. teach *Bacillus subtilis* NB22 as the microbe to ferment and obtain ItA or its homologues from soybean extract, but does not teach *Bacillus subtilis* SD142 or a mutant of *Bacillus subtilis* SD142. As mention above, the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not applicants' *Bacillus subtilis* SD142 or a mutant of *Bacillus subtilis* SD142 differs and, if so, to what extent from the *Bacillus subtilis* NB22 discussed in the references. Accordingly, it has been established that the prior art strains, which have, the same genus and species classification and share the property of being able to produce, ItA and its homologues demonstrate a reasonable probability that it is either identical or sufficiently similar that whatever differences exist are not patentably significant. Therefore, the burden of establishing novelty or unobviousness by objective evidence is shifted to applicants.

Also Phae et al. is silent on how much, if at any, surfactin is produce by *B. subtilis* NB22. The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether *B. subtilis* NB22 differs and, if so, to what extent this strain produces surfactin. Accordingly, it has been established that the prior art (See Pg 4 and 5 of Final Office Action mailed 6/6/08) that *B. subtilis* NB22 which has

the same genus and species classification and share the property of producing ItA and makes no mention of simultaneously producing of surfactin demonstrate a reasonable probability that it is either identical or sufficiently similar that whatever differences exist are not patentably significant. Therefore, the burden of establishing novelty or unobviousness by objective evidence is shifted to Applicants. Also see pages 5 and 6 of the Final Office Action (mailed 6/6/08) that discusses how HPLC analysis shows no sign of surfactin but multiple analogs of Iturin A.

While Phae et al. does teach the steps claimed in the method but does not teach that their microbe can produce ItA at concentrations of 1.5 g/L. However, one of ordinary skill in the art would recognize that yield of product is a result effective variable based on experimental conditions such a pH, aeration rate, temperature, reaction time (Phae et al. Figures 2-5). Absent any teaching of criticality by the applicant concerning this yield of ItA, it would be *prima facie* obvious that one of ordinary skill in the art would recognize these limitations are result effective variables which can be met as a matter of routine optimization (M.P.E.P. § 2144.05 II). Furthermore, evidence of criticality such as unexpected results must be commensurate with the scope of the claims including the conditions from which those results were obtained (M.P.E.P. § 716.02 (a) and (d)).

Therefore claims 1-9 are obvious in view of the above reference.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phea et al. and supporting references as applied to claims 1-9 above, and further in view of Ohno#1.



The descriptions of claims 1-9 are recited in the 35 U.S.C § 103 rejection above and are applied here as well.

Like Phea et al. Ohno#1 also teach the fermentation of *B. subtilis* NB22 on the soybean extract okara using the similar culture medium as Phae et al. which consist of glucose, and  $\text{KH}_2\text{PO}_4$  as additional nutrients (Ohno#1, col 1, lines 1-15). In the method of Ohno#1, 3 mL of *Bacillus subtilis* NB22 was suspended in 3S medium (page 802, col 2, Preparation of seeding culture). The total volume of liquid media added to the okara fermentation is 4.1 mL (Ohno#1, pg 803, col 1). This fermentation method produce okara at a yield of 1.65 g of ItA/kg okara (pg 805, col 1). Since 15 g of okara were used in this fermentation of example of Ohno#1 , 24.75 g of ItA and its homologues were produced. Since the liquid medium added to the fermentation process was 4.1 mL this provides an ItA concentration of 6 g/mL or 6000 g/L that the *Bacillus subtilis* NB22 microbes were able to produce (see Figure 3). Indeed Ohno#1 shows that high yields of ItA/kg okara can be achieved with more moisture in their substrate (Ohno#1, Figure 7). Now while Ohno#1 uses a solid substrate fermentation method using a soybean extract with minimal amounts of medium it would be obvious to try to scale the method of Ohno#1 to a liquid fermentation method by adding more liquid media since *B. subtilis* NB22 has been successfully cultured and shown to produce ItA by Phae et al.

Furthermore, Ohno#1 teach that solid cultures of *B. subtilis* NB22 can be obtained and placed on fields as a fertilizer (Ohno#1, pg 805, col 2). Obviously one of ordinary skill in the art would recognize that solid cultures are dried or at the very least not a solution so much of the media would need to be removed.

Therefore claims 1-10 are obvious in view of the above references.

No claims are currently allowed in this application.

**In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure**, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

#### CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Thane Underdahl  
Art Unit 1651

/Leon B Lankford/  
Primary Examiner, Art Unit 1651